REMARKS

Entry of the foregoing, reexamination, and further and favorable reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

I. Claim Amendments

By the foregoing amendment, claims 1, 3, 5-7, 11-15, 18, and 24-26 have been amended; claims 2 and 10 have been canceled; and new claim 27 has been added.

Specifically, claim 1 has been amended to recite that the poxviral particle is an intracellular mature virus (IMV) vaccinia virus particle. Support for this amendment can be found throughout the specification and claims as filed, for example in original claims 2 (vaccinia virus) and 9 (IMV).

Claim 1 has also been amended to recite that the at least one ligand moiety comprises an antibody fragment or a binding moiety of a normal cell surface receptor. Antibody fragments and binding moieties of normal cell surface receptors are supported at least at page 8, lines 19-27 and at page 9, lines 23-25, respectively.

Claim 1 has been further amended to recite that the antibody fragment or binding moiety of a normal cell surface receptor is fused to the N-terminus of the expression product of the vaccinia virus A27L gene, so as to produce a chimeric polypeptide expressed at the surface of the IMV vaccinia virus particle. This amendment is supported at least at page 6, lines 3-4 and 17-22; in original claim 10; and in the Examples.

In addition, claim 1 has been amended to recite that the anti-ligand molecule is a cell-specific marker, a tissue-specific marker, a viral antigen, or a tumor-associated marker, as

supported at least at page 7, lines 21-23; page 8, lines 17-19; and page 10, lines 5-8 of the specification.

Claim 5 has been amended to correspond to claim 1 by replacing the phrase "said ligand moiety binds a tumor-specific antigen" with the phrase "said anti-ligand molecule is a tumor-associated marker."

New claim 27 depends from claim 5 and recites the particular tumor-associated markers that were previously recited in claim 5.

Claims 5 and 26 have been amended by deleting the term "differentially expressed."

Other amendments to the claims have been made to clarify the claim language and bring the claims into better conformance with U.S. patent practice. These amendments are merely editorial in nature and are not intended to change the scope of the claims or any elements recited therein.

The amendments to the claims, including cancellation of claims, have been made without prejudice or disclaimer to any subject matter recited or canceled canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments of the above-identified application are respectfully requested.

II. Response to Claim Rejections Under 35 U.S.C. § 112, First Paragraph – Enablement

At pages 2-4 of the Office Action, the rejection of claims 1-3, 5, 6, 10-15, 18, and 24-26 under 35 U.S.C. § 112, first paragraph, as purportedly lacking enablement, has been maintained.

Specifically, the Examiner has stated that claim 1 is lacking the limitations required to practice the claimed invention, because in order for the recited poxviral particle to have the claimed targeted infection specificity, the target cell must comprise an appropriate target (such as an overexpressed cellular protein). The Examiner has also stated that claim 5 is not enabled, because the term "differentially expressed" can mean either underexpressed or overexpressed, and the method requires overexpression of the anti-ligand.

This rejection is respectfully traversed, for at least the following reasons.

Initially, Applicants note that to expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, the claims have been amended as described above. In particular, claim 1 has been amended to specifically recite the anti-ligand molecules that are disclosed in the specification (namely cell-specific markers, tissue-specific markers, and tumor-associated markers). Applicants submit that cell-specific markers, tissue-specific markers, and tumor-associated markers are all appropriate targets for the recited IMV vaccinia virus particle.

In particular, a person of ordinary skill in the art would know how to make and use IMV vaccinia virus particles having a targeted infection specificity to target cells having cell-specific markers, tissue-specific markers, or tumor-associated markers localized at the cell surface. In this regard, Applicants note that contrary to the Examiner's assertion, targeted infection specificity does not necessarily require "overexpression" of the anti-ligand molecule. In fact, the term "overexpressed" implies an abnormally high expression, for example abnormally high expression that is due to a disease state such as cancer. The present invention does encompass virus particles having an infection specificity toward cells that overexpress an anti-ligand molecule. However, as disclosed in the specification and readily recognized by a person of ordinary skill in the art, targeted infection specificity can also

depend on normal "differential" or "specific" expression in one or more cell types. For example, targeted infection specificity could be based on the normal expression of cell-specific or tissue-specific markers, such as the LDL receptor that is specifically expressed in normal liver cells (*see, e.g.* page 11, lines 10-15 of the present specification). Thus, the enablement requirement is met for the entire scope of the claims.

In addition, to expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, claims 5 and 26 have been amended by deleting the term "differentially expressed."

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

III. Response to Claim Rejections Under 35 U.S.C. § 112, First Paragraph – Written Description

At pages 4-6 of the Office Action, claims 1-3, 5, 6, 10-15, 18, and 24-26 have been rejected under 35 U.S.C. § 112, first paragraph, as purportedly failing to comply with the written description requirement.

Specifically, the Examiner has stated that because the polypeptide ligand molecule recited in claim 1 is defined solely in terms of function (e.g. "a ligand moiety") rather than structure, a person of ordinary skill in the art would not know which polypeptides would function as ligands in the present invention.

This rejection is respectfully traversed, for at least the following reasons.

In order to expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, claim 1 has been amended to recite that the ligand moiety comprises an antibody fragment or a binding moiety of a natural cell-surface receptor.

Information which is known in the art need not be described in detail in the specification (*see, e.g. Hybritech, Inc v. Monoclonal Antibodies, Inc.,* 231 USPQ 81, 90 (Fed. Cir. 1986)). In addition, satisfaction of the written description requirement does not require either recitation or incorporation by reference of publicly accessible sequences (*see, e.g. Falkner v. Ingles*, 79 USPQ2d 1001 (Fed. Cir. 2006) and *Capon v. Eshhar*, 76 USPQ 1078 (Fed. Cir. 2005)).

With regard to the present application, Applicants submit that antibody fragments and binding moieties of natural cell-surface receptors were well known and had been extensively studied as of the filing date of the present application. In particular, numerous literature references describing such polypeptides were available, and a person of ordinary skill in the art would have reasonably expected the recited polypeptide ligands to function in the claimed invention. In addition, a representative number of antibody fragments (*see, e.g.*, pages 8-10) and binding moieties of natural cell-surface receptors (*see, e.g.*, page 11, lines 12-24 and 30-33) are also set forth in the specification. Thus, the present application, along with the prior art at the time of filing, provided sufficient information to envisage which antibody fragments and binding moieties of natural cell-surface receptors would be suitable for the present invention.

Hence, Applicants submit that the written description requirement is met for the entire scope of the claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

IV. Response to Claim Rejections Under 35 U.S.C. § 102

At pages 6-7 of the Office Action, claims 1-3, 5, 6, 10, 11, 18, and 24-26 have been rejected under 35 U.S.C. § 102(b) as purportedly being anticipated by Balloul et al. (Cellular

and Molecular Biology 40, 49-59 (1994)) as evidenced by Vazquez et al. (Journal of Virology 72, 1-23 (1998)).

According to the Examiner, Balloul et al. discloses a chimeric poxviral particle expressing IL-2 and a polypeptide that binds to MUC-1 antigen on a tumor cell. The Examiner acknowledges that the reference does not expressly disclose that the ligand moiety is fused to the A27L gene product. However, the Examiner has concluded that one would expect that the current particles and the reference particles are the same.

This rejection is respectfully traversed.

It is well established that for prior art to be anticipatory, every element of the claimed invention must be disclosed in a single item of prior art in the form literally defined in the claim. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 213 U.S.P.Q. 81, 90 (Fed. Cir. 1986). Applicants submit that the cited reference fails to satisfy this requirement, for at least the following reasons.

The present claims are directed to an IMV vaccinia virus particle comprising an antibody fragment or binding moiety of a normal cell surface receptor fused to the N-terminus of the expression product of the vaccinia virus A27L gene, so as to produce a chimeric polypeptide localized at the surface of the vaccinia virus.

In contrast, Balloul et al. discloses a double recombinant vaccinia virus co-expressing the MUC-1 gene and a cytokine gene (IL-2, IL-4, IL-5, IL-6 or IL-7) as an adjuvant. The cytokine-encoding gene is inserted in the tk locus of the vaccinia virus genome (Figure 2 and top of p51, second column), and the MUC-1-encoding gene is inserted in the K1L locus (Figure 2 and last paragraph, p51, second column). Applicants further note that in contrast to the A27L gene of the present invention, neither the tk locus nor the K1L locus encode a surface-exposed polypeptide. Accordingly, neither MUC-1 nor the cytokine are expressed as

chimeric polypeptides at the surface of the vaccinia virus. Instead, the MUC-1 polypeptide is anchored in the membrane of the infected cells due to the presence of a trans-membrane domain in its sequence (see the third paragraph, second column on page 53), and the cytokine is secreted into the external medium due to an N-terminal signal peptide.

In addition, because the reference p14 protein (*i.e.* the expression product of the A27L gene) is wildtype, the vaccinia virus particles disclosed by Balloul et al. are not targeted, and can infect any cell normally permissive to vaccinia infection.

Finally, in further contrast to the present invention, the reference particle expresses the MUC-1 tumor-associated antigen itself, rather than a ligand of MUC-1 as in the examples set forth in the present application.

Accordingly, the reference does not teach or even suggest the subject matter recited in the present claims, and Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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Date: May 30, 2007

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